

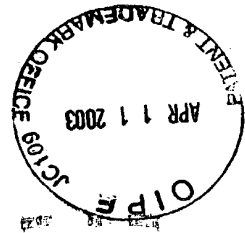
2459-1-003 CIP

# Structure-based sequence homology alignment of bromodomains

## ZA Loop

	720	740	760	780	800	820
	$\alpha_A$	$\alpha_B$	$\alpha_C$	$\alpha_D$	$\alpha_E$	$\alpha_F$
hsp/cap	719- SKPRDPTQLYSTLSLQVKSQ	719- SKPRDPTQLYSTLSLQVKSQ	719- SKPRDPTQLYSTLSLQVKSQ	719- SKPRDPTQLYSTLSLQVKSQ	719- SKPRDPTQLYSTLSLQVKSQ	719- SKPRDPTQLYSTLSLQVKSQ
hucg5	363- GKELKDPDQVLTUKNLAQKSH	363- GKELKDPDQVLTUKNLAQKSH	363- GKELKDPDQVLTUKNLAQKSH	363- GKELKDPDQVLTUKNLAQKSH	363- GKELKDPDQVLTUKNLAQKSH	363- GKELKDPDQVLTUKNLAQKSH
tlp55	280- LKSKERSTNQCANIEMKHHQ	280- LKSKERSTNQCANIEMKHHQ	280- LKSKERSTNQCANIEMKHHQ	280- LKSKERSTNQCANIEMKHHQ	280- LKSKERSTNQCANIEMKHHQ	280- LKSKERSTNQCANIEMKHHQ
sgcn5	324- AORPKRCHDAIAQNIITELQNA	324- AORPKRCHDAIAQNIITELQNA	324- AORPKRCHDAIAQNIITELQNA	324- AORPKRCHDAIAQNIITELQNA	324- AORPKRCHDAIAQNIITELQNA	324- AORPKRCHDAIAQNIITELQNA
hsp300	1046- KKIEKPELROALMPTLEALYRD	1046- KKIEKPELROALMPTLEALYRD	1046- KKIEKPELROALMPTLEALYRD	1046- KKIEKPELROALMPTLEALYRD	1046- KKIEKPELROALMPTLEALYRD	1046- KKIEKPELROALMPTLEALYRD
hscbp	1082- KKIEKPELROALMPTLEALYRD	1082- KKIEKPELROALMPTLEALYRD	1082- KKIEKPELROALMPTLEALYRD	1082- KKIEKPELROALMPTLEALYRD	1082- KKIEKPELROALMPTLEALYRD	1082- KKIEKPELROALMPTLEALYRD
mcbp	1083- KKIEKPELROALMPTLEALYRD	1083- KKIEKPELROALMPTLEALYRD	1083- KKIEKPELROALMPTLEALYRD	1083- KKIEKPELROALMPTLEALYRD	1083- KKIEKPELROALMPTLEALYRD	1083- KKIEKPELROALMPTLEALYRD
cey31	861- DTVFSQEDLTKPLPWEKLDKSE	861- DTVFSQEDLTKPLPWEKLDKSE	861- DTVFSQEDLTKPLPWEKLDKSE	861- DTVFSQEDLTKPLPWEKLDKSE	861- DTVFSQEDLTKPLPWEKLDKSE	861- DTVFSQEDLTKPLPWEKLDKSE
hscg1-1	1376- RRTDPMVTLSSIESITNNRDL	1376- RRTDPMVTLSSIESITNNRDL	1376- RRTDPMVTLSSIESITNNRDL	1376- RRTDPMVTLSSIESITNNRDL	1376- RRTDPMVTLSSIESITNNRDL	1376- RRTDPMVTLSSIESITNNRDL
hscg1-1	1371- RRTDPMVTLSSIESITNNRDL	1371- RRTDPMVTLSSIESITNNRDL	1371- RRTDPMVTLSSIESITNNRDL	1371- RRTDPMVTLSSIESITNNRDL	1371- RRTDPMVTLSSIESITNNRDL	1371- RRTDPMVTLSSIESITNNRDL
hscg1-2	1498- LUDDDQVAFSPILNITVORNAV	1498- LUDDDQVAFSPILNITVORNAV	1498- LUDDDQVAFSPILNITVORNAV	1498- LUDDDQVAFSPILNITVORNAV	1498- LUDDDQVAFSPILNITVORNAV	1498- LUDDDQVAFSPILNITVORNAV
hscg1-2	1493- LUDDDQVAFSPILNITVORNAV	1493- LUDDDQVAFSPILNITVORNAV	1493- LUDDDQVAFSPILNITVORNAV	1493- LUDDDQVAFSPILNITVORNAV	1493- LUDDDQVAFSPILNITVORNAV	1493- LUDDDQVAFSPILNITVORNAV
hsking1-1	24- KRCRTVQLQYLRVWHLAKHQ	24- KRCRTVQLQYLRVWHLAKHQ	24- KRCRTVQLQYLRVWHLAKHQ	24- KRCRTVQLQYLRVWHLAKHQ	24- KRCRTVQLQYLRVWHLAKHQ	24- KRCRTVQLQYLRVWHLAKHQ
hsofx-1	31- KRCRTVQLQYLRVWHLAKHQ	31- KRCRTVQLQYLRVWHLAKHQ	31- KRCRTVQLQYLRVWHLAKHQ	31- KRCRTVQLQYLRVWHLAKHQ	31- KRCRTVQLQYLRVWHLAKHQ	31- KRCRTVQLQYLRVWHLAKHQ
dmfsh-1	31- KRCRTVQLQYLRVWHLAKHQ	31- KRCRTVQLQYLRVWHLAKHQ	31- KRCRTVQLQYLRVWHLAKHQ	31- KRCRTVQLQYLRVWHLAKHQ	31- KRCRTVQLQYLRVWHLAKHQ	31- KRCRTVQLQYLRVWHLAKHQ
scbdf1-1	148- NP1PKHQKHALAKAVARKL	148- NP1PKHQKHALAKAVARKL	148- NP1PKHQKHALAKAVARKL	148- NP1PKHQKHALAKAVARKL	148- NP1PKHQKHALAKAVARKL	148- NP1PKHQKHALAKAVARKL
hsking1-2	295- KKGKLSKHLKCHGILKELSKH	295- KKGKLSKHLKCHGILKELSKH	295- KKGKLSKHLKCHGILKELSKH	295- KKGKLSKHLKCHGILKELSKH	295- KKGKLSKHLKCHGILKELSKH	295- KKGKLSKHLKCHGILKELSKH
hsofx-2	304- KKGKLSKHLKCHGILKELSKH	304- KKGKLSKHLKCHGILKELSKH	304- KKGKLSKHLKCHGILKELSKH	304- KKGKLSKHLKCHGILKELSKH	304- KKGKLSKHLKCHGILKELSKH	304- KKGKLSKHLKCHGILKELSKH
dmfsh-2	473- KKGKLSKHLKCHGILKELSKH	473- KKGKLSKHLKCHGILKELSKH	473- KKGKLSKHLKCHGILKELSKH	473- KKGKLSKHLKCHGILKELSKH	473- KKGKLSKHLKCHGILKELSKH	473- KKGKLSKHLKCHGILKELSKH
hsofx1-2	311- KKGKLSKHLKCHGILKELSKH	311- KKGKLSKHLKCHGILKELSKH	311- KKGKLSKHLKCHGILKELSKH	311- KKGKLSKHLKCHGILKELSKH	311- KKGKLSKHLKCHGILKELSKH	311- KKGKLSKHLKCHGILKELSKH
hsk140	626- MEMQUTPLILLKRTLEQLOKDTG	626- MEMQUTPLILLKRTLEQLOKDTG	626- MEMQUTPLILLKRTLEQLOKDTG	626- MEMQUTPLILLKRTLEQLOKDTG	626- MEMQUTPLILLKRTLEQLOKDTG	626- MEMQUTPLILLKRTLEQLOKDTG
hscmap	594- SEQOFAIQAKKIMAILWVRAAN	594- SEQOFAIQAKKIMAILWVRAAN	594- SEQOFAIQAKKIMAILWVRAAN	594- SEQOFAIQAKKIMAILWVRAAN	594- SEQOFAIQAKKIMAILWVRAAN	594- SEQOFAIQAKKIMAILWVRAAN
gufb1-1	41- NLPYVDPVAVCHELNTIRYKQDQ	41- NLPYVDPVAVCHELNTIRYKQDQ	41- NLPYVDPVAVCHELNTIRYKQDQ	41- NLPYVDPVAVCHELNTIRYKQDQ	41- NLPYVDPVAVCHELNTIRYKQDQ	41- NLPYVDPVAVCHELNTIRYKQDQ
gufb1-2	174- SSICVLKELLOLEAVAVATN	174- SSICVLKELLOLEAVAVATN	174- SSICVLKELLOLEAVAVATN	174- SSICVLKELLOLEAVAVATN	174- SSICVLKELLOLEAVAVATN	174- SSICVLKELLOLEAVAVATN
gufb1-3	374- TSMUTSPPLQYLYUTVASCNNQ	374- TSMUTSPPLQYLYUTVASCNNQ	374- TSMUTSPPLQYLYUTVASCNNQ	374- TSMUTSPPLQYLYUTVASCNNQ	374- TSMUTSPPLQYLYUTVASCNNQ	374- TSMUTSPPLQYLYUTVASCNNQ
gufb1-4	511- KRMHMKQKMLKLYNAVLEARESG	511- KRMHMKQKMLKLYNAVLEARESG	511- KRMHMKQKMLKLYNAVLEARESG	511- KRMHMKQKMLKLYNAVLEARESG	511- KRMHMKQKMLKLYNAVLEARESG	511- KRMHMKQKMLKLYNAVLEARESG
gufb1-5	647- KSKYMTMPOOKLYEYAVRYTQ	647- KSKYMTMPOOKLYEYAVRYTQ	647- KSKYMTMPOOKLYEYAVRYTQ	647- KSKYMTMPOOKLYEYAVRYTQ	647- KSKYMTMPOOKLYEYAVRYTQ	647- KSKYMTMPOOKLYEYAVRYTQ
spnro-1	5- HNAPEOKTKFDEVEALVGLANE	5- HNAPEOKTKFDEVEALVGLANE	5- HNAPEOKTKFDEVEALVGLANE	5- HNAPEOKTKFDEVEALVGLANE	5- HNAPEOKTKFDEVEALVGLANE	5- HNAPEOKTKFDEVEALVGLANE
spnro-2	138- GTNEIDVHKVQNTILOALHEKQDQ	138- GTNEIDVHKVQNTILOALHEKQDQ	138- GTNEIDVHKVQNTILOALHEKQDQ	138- GTNEIDVHKVQNTILOALHEKQDQ	138- GTNEIDVHKVQNTILOALHEKQDQ	138- GTNEIDVHKVQNTILOALHEKQDQ
ssn2a	1377- SPNPKLTKONNAIITVINYKQSS	1377- SPNPKLTKONNAIITVINYKQSS	1377- SPNPKLTKONNAIITVINYKQSS	1377- SPNPKLTKONNAIITVINYKQSS	1377- SPNPKLTKONNAIITVINYKQSS	1377- SPNPKLTKONNAIITVINYKQSS
hbrg1	1418- SPNPKLTKONNAIITVINYKQSS	1418- SPNPKLTKONNAIITVINYKQSS	1418- SPNPKLTKONNAIITVINYKQSS	1418- SPNPKLTKONNAIITVINYKQSS	1418- SPNPKLTKONNAIITVINYKQSS	1418- SPNPKLTKONNAIITVINYKQSS
gubg1	1373- SHPPKLTORNAIITVINYKQSS	1373- SHPPKLTORNAIITVINYKQSS	1373- SHPPKLTORNAIITVINYKQSS	1373- SHPPKLTORNAIITVINYKQSS	1373- SHPPKLTORNAIITVINYKQSS	1373- SHPPKLTORNAIITVINYKQSS
gubg1	1436- SHPPKLTORNAIITVINYKQSS	1436- SHPPKLTORNAIITVINYKQSS	1436- SHPPKLTORNAIITVINYKQSS	1436- SHPPKLTORNAIITVINYKQSS	1436- SHPPKLTORNAIITVINYKQSS	1436- SHPPKLTORNAIITVINYKQSS
hstf1b	694- AKISPAKCKRCERVALLPCH	694- AKISPAKCKRCERVALLPCH	694- AKISPAKCKRCERVALLPCH	694- AKISPAKCKRCERVALLPCH	694- AKISPAKCKRCERVALLPCH	694- AKISPAKCKRCERVALLPCH
hstf1b	694- AKISPAKCKRCERVALLPCH	694- AKISPAKCKRCERVALLPCH	694- AKISPAKCKRCERVALLPCH	694- AKISPAKCKRCERVALLPCH	694- AKISPAKCKRCERVALLPCH	694- AKISPAKCKRCERVALLPCH
hstf1a	865- TKITPTDKRCERLLPCH	865- TKITPTDKRCERLLPCH	865- TKITPTDKRCERLLPCH	865- TKITPTDKRCERLLPCH	865- TKITPTDKRCERLLPCH	865- TKITPTDKRCERLLPCH

Figure 1





09794553 041102

2459-1-003 CIP

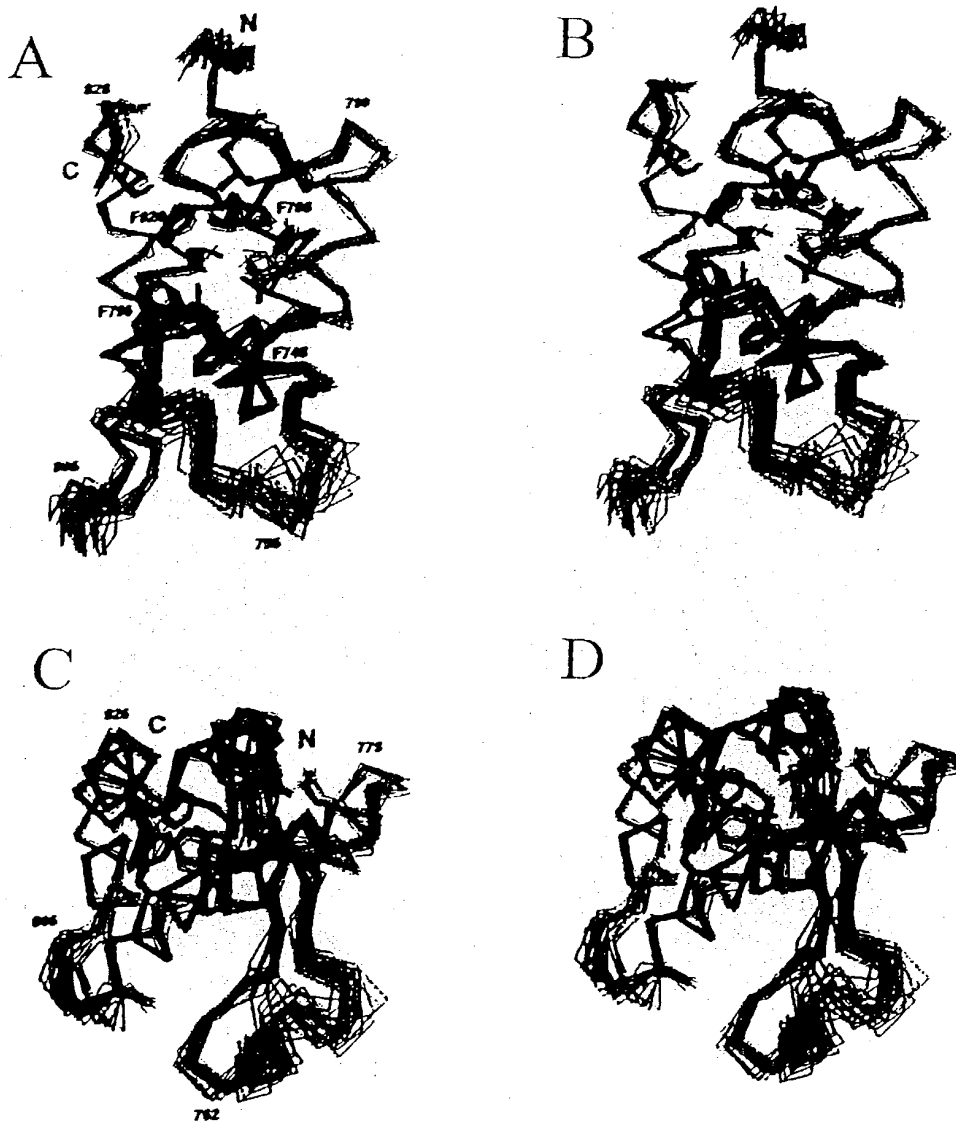


Figure 2A-2D



00784552 041103

2459-1-003 CIP

### Three-Dimensional Structure of the P/CAF Bromodomain

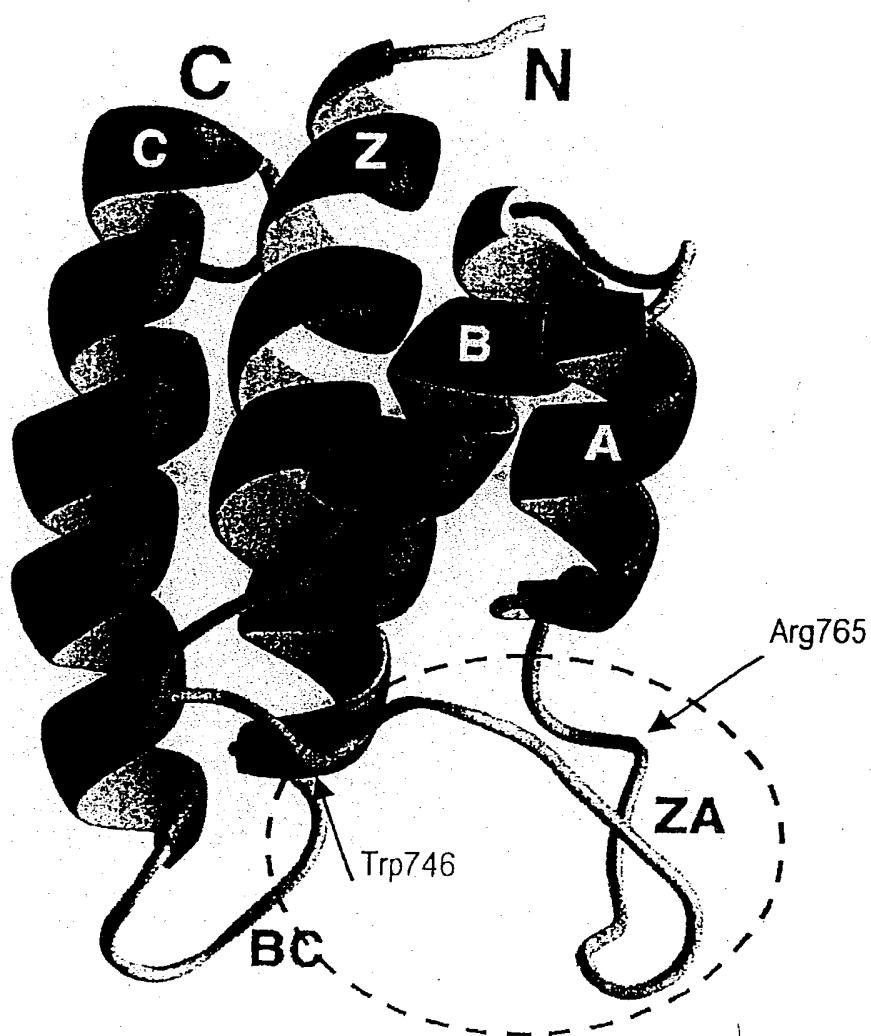


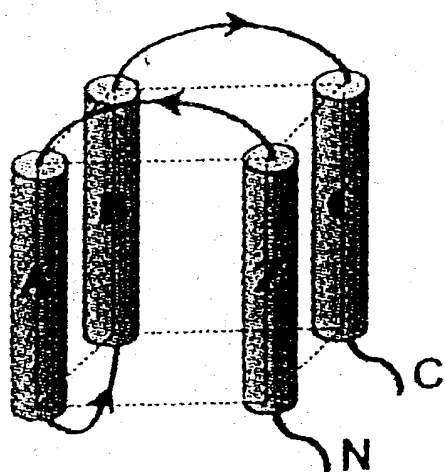
Figure 2E



00724553-041103

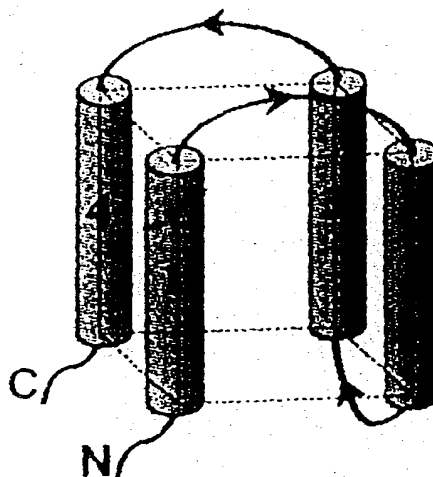
2459-1-003 CIP

F



Left-handed bundle

G



Right-handed bundle

Figure 2F-2G



2459-1-003 CIP

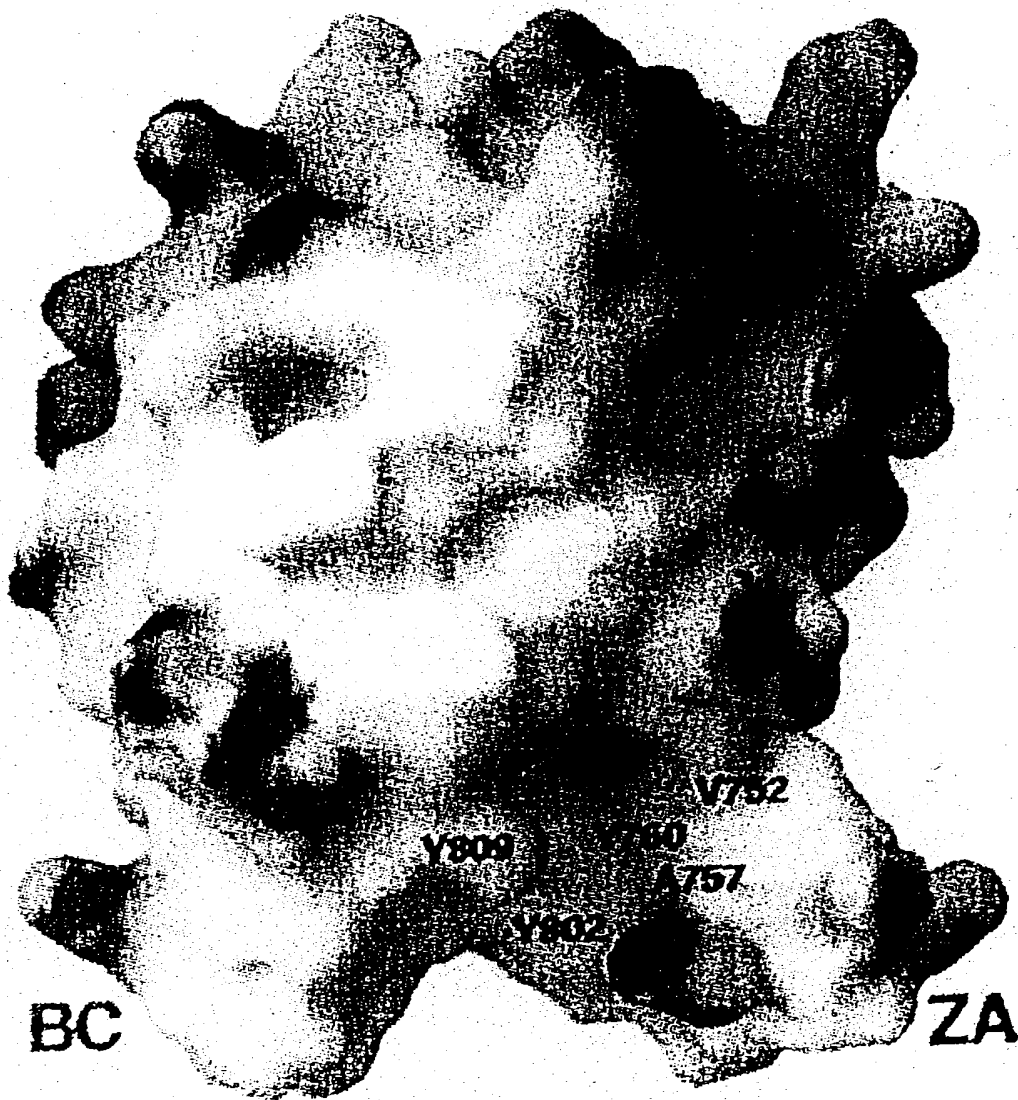


Figure 2H



2459-1-003 CIP

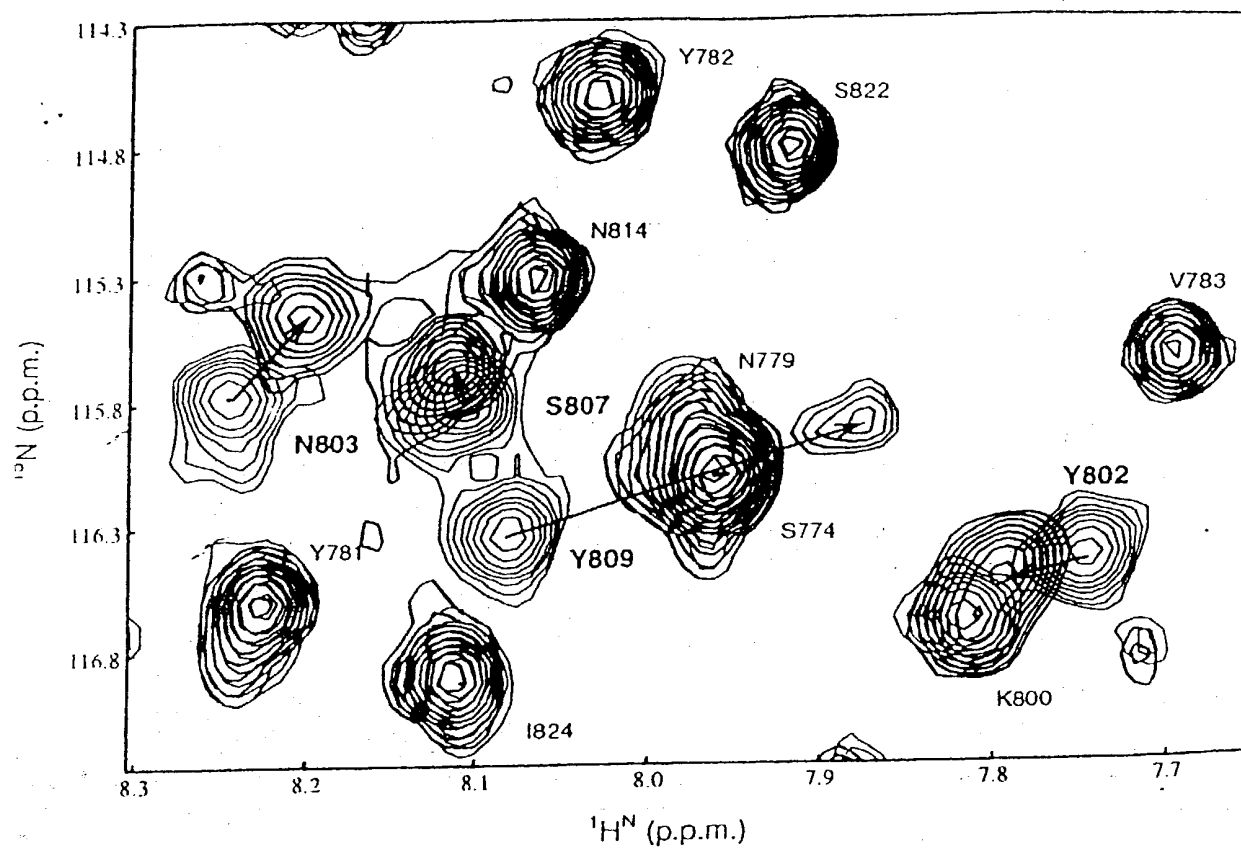


Figure 3A



2459-1-003 CIP

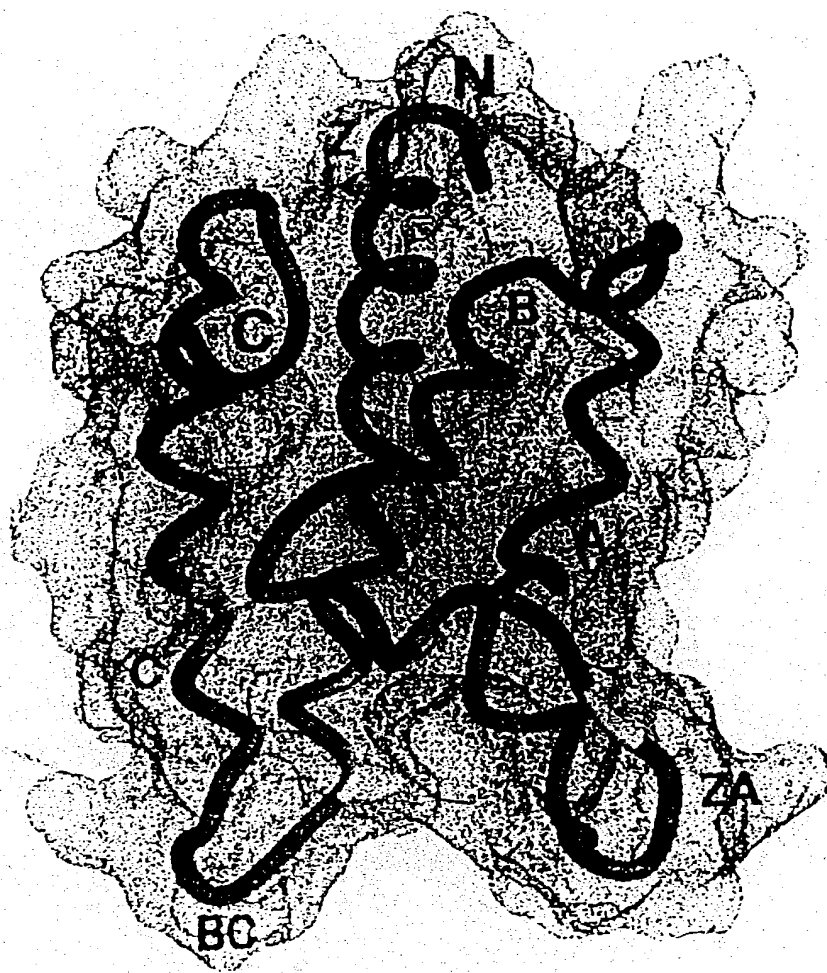
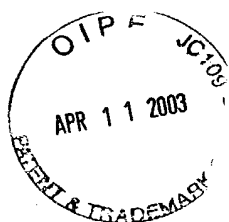
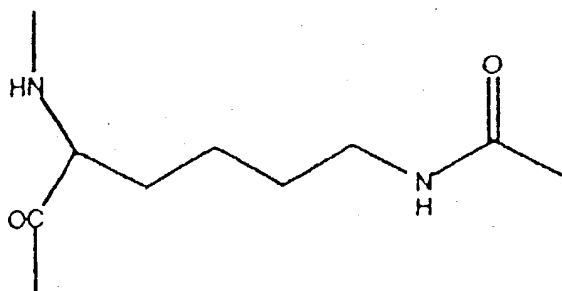


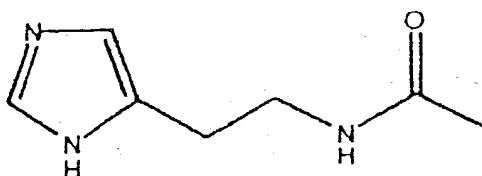
Figure 3B



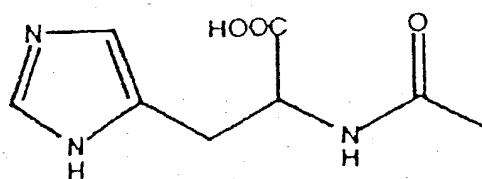
2459-1-003 CIP



*N*ε-acetyl-lysine



*N*ω-acetyl-histamine



*N*α-acetyl-histidine

Figure 3C





00794553 .041103

2459-1-003 CIP

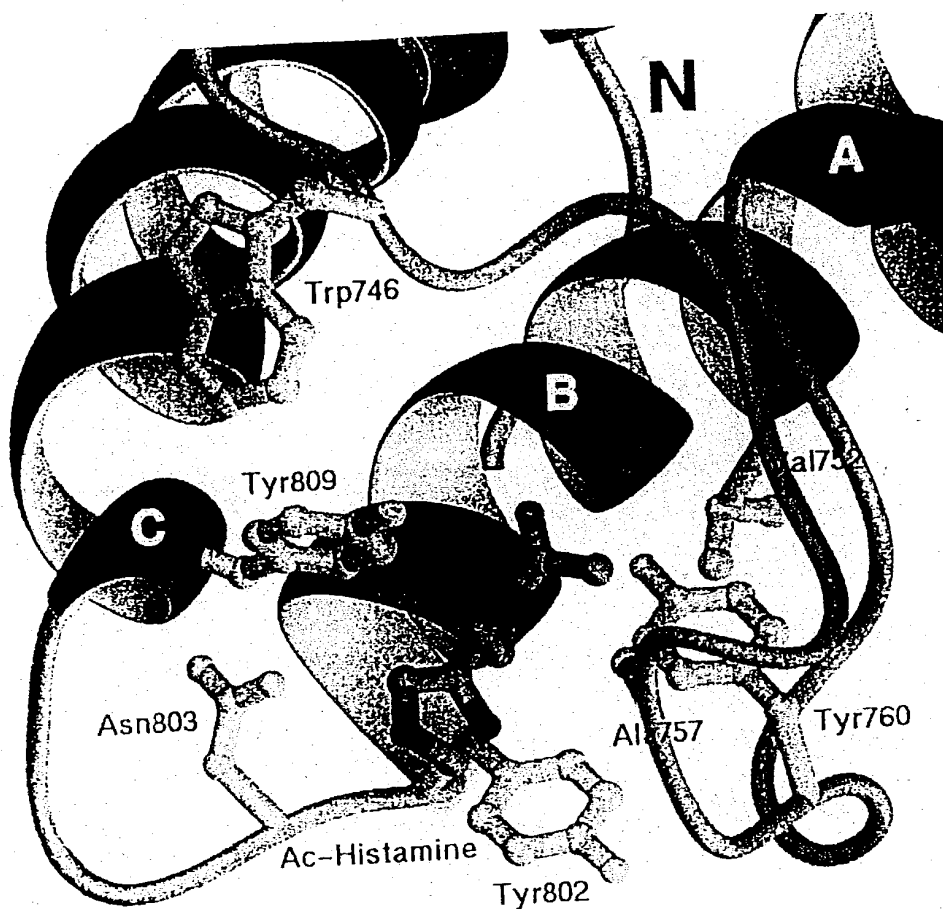


Figure 4



2459-1-003 CIP

2459-1-003 CIP

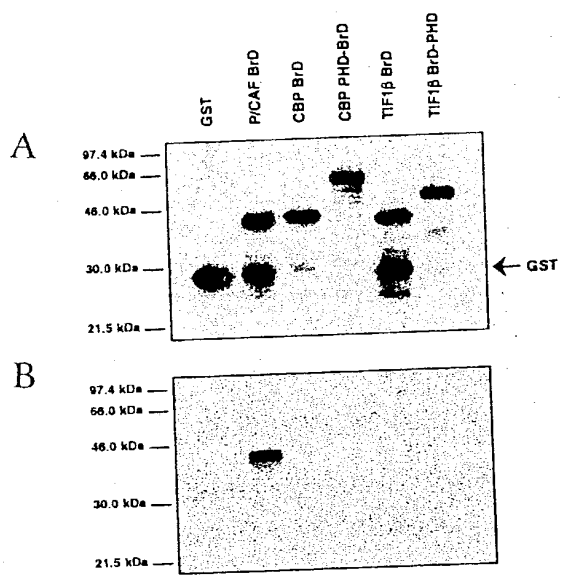


Figure 5



2459-1-003 CIP

2459-1-003 CIP

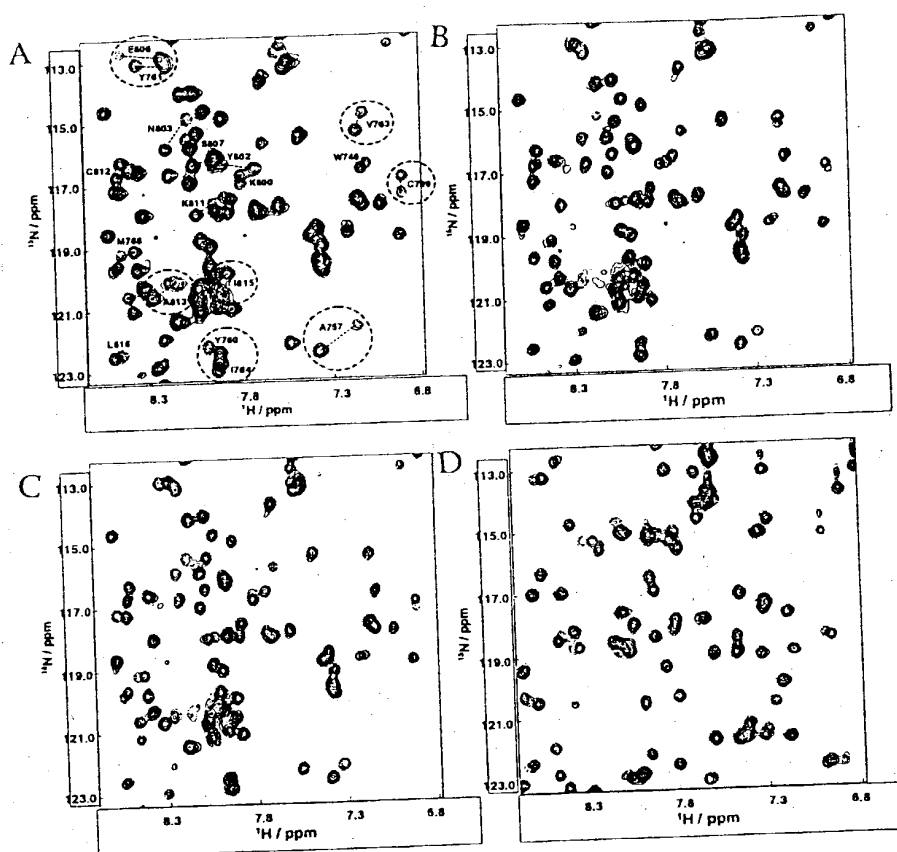


Figure 6



2459-1-003 CIP

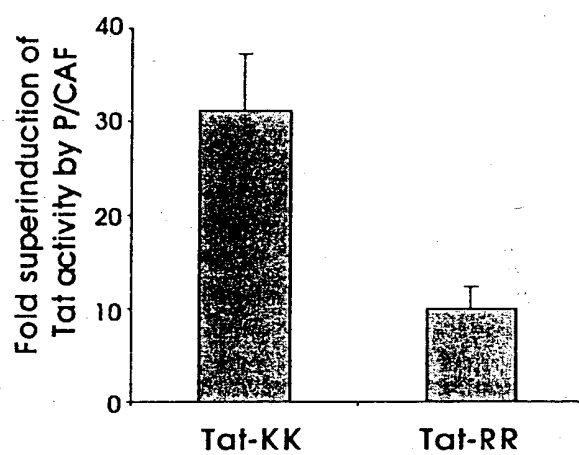
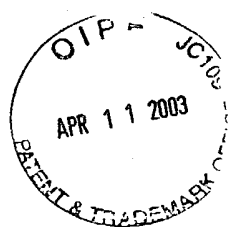


Figure 7



00794552 044333

2459-1-003 CIP

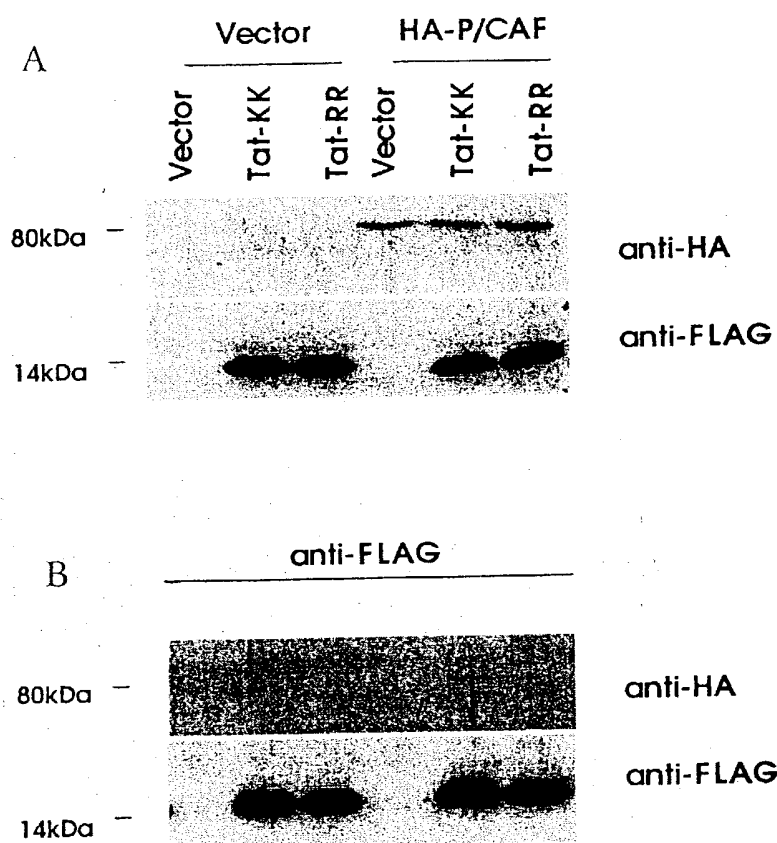
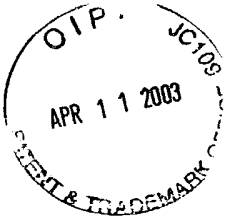
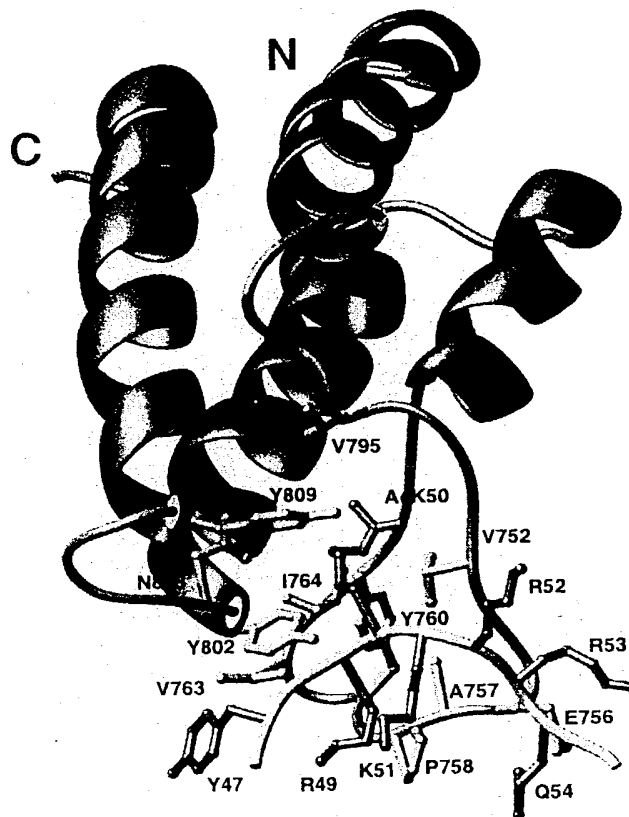


Figure 8



2459-1-003 CIP



HIV-1 Tat Peptide: SYGR-AcK-KRRQRC

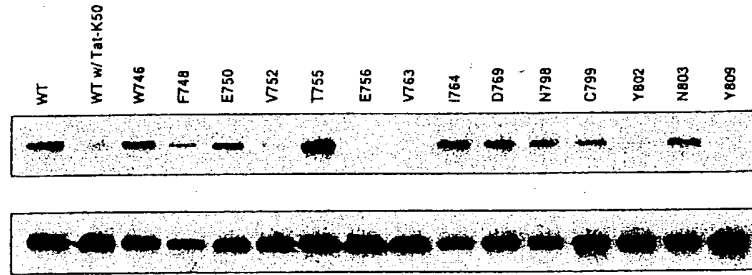
Figure 9



2459-1-003 CIP

2459-1-003 CIP

A



B

- |                          |                          |
|--------------------------|--------------------------|
| 1. Control               | SYGR-K-KRRQRC            |
| 2. Tat_K50 (aa 46-55)    | SYGR-AcK-KRRQRC          |
| 3. Tat_AcK50             | SAGR-AcK-KRRQRC          |
| 4. Tat_AcK50_Y47A        | SYGA-AcK-KRRQRC          |
| 5. Tat_AcK50_R49A        | SYGR-AcK-ARRQRC          |
| 6. Tat_AcK50_K51A        | SYGR-AcK-KARQRC          |
| 7. Tat_AcK50_R52A        | SYGR-AcK-KRAQRC          |
| 8. Tat_AcK50_R53A        | SYGR-AcK-KRRARC          |
| 9. Tat_AcK50_Q54A        | SYGRK-AcK-RRQRC          |
| 10. Tat_AcK51            | TNCYCK-AcK-CCFH          |
| 11. Tat_AcK28 (aa 23-33) | SGRGKGGKGLGKGGA-AcK-RHRK |
| 12. Histone H4_AcK16     |                          |

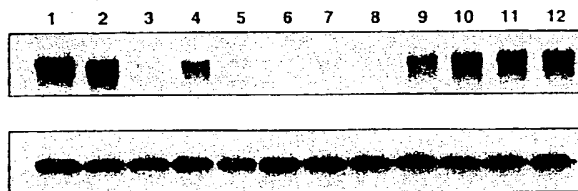
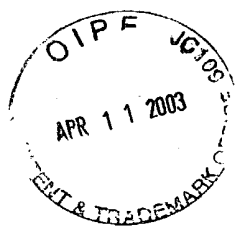


Figure 10



2459-1-003 CIP

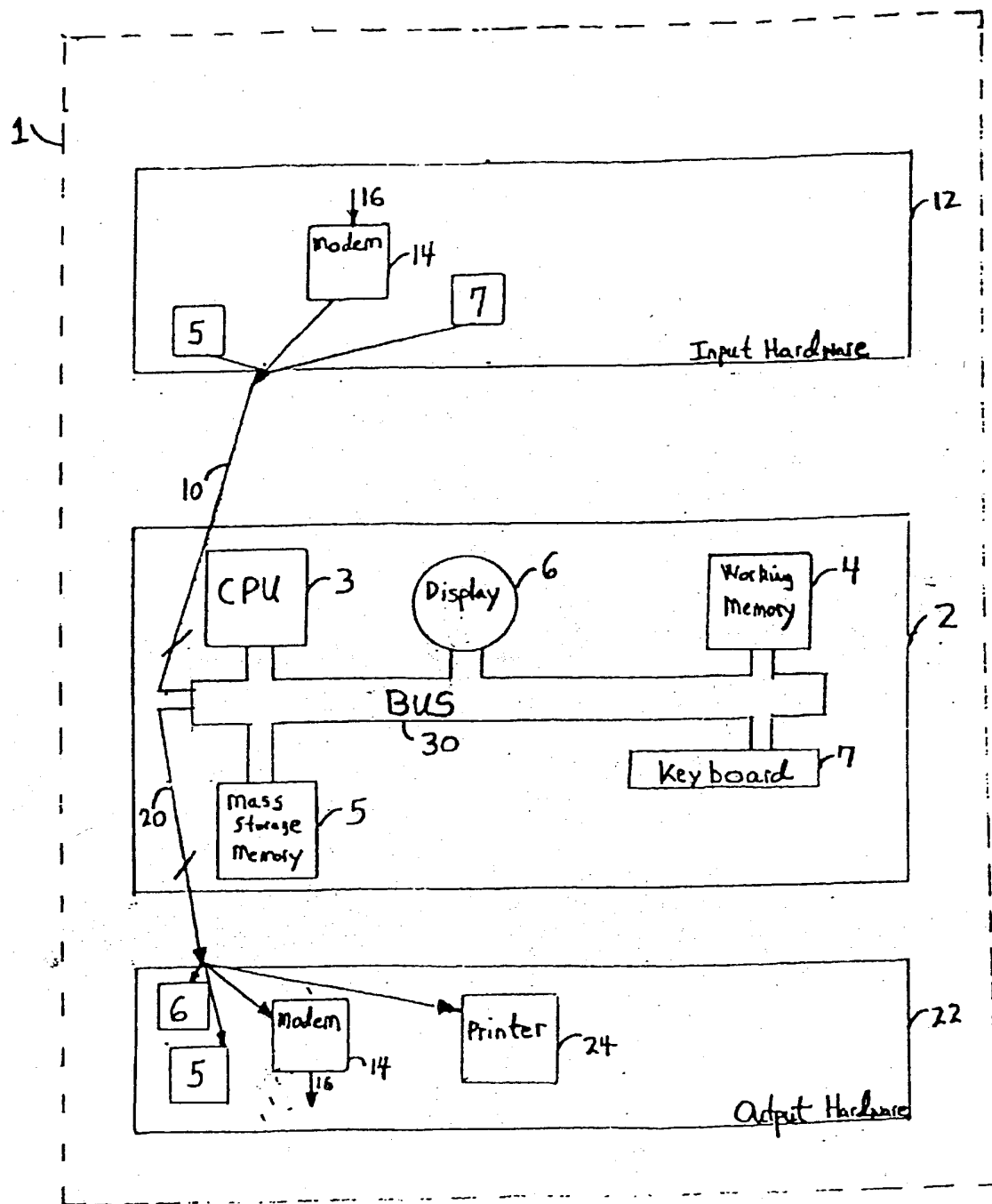
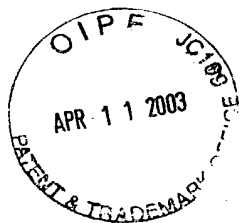
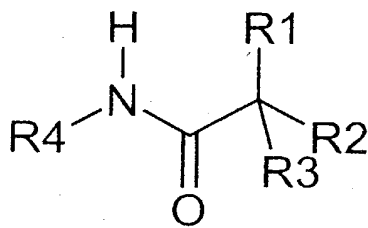


Figure 11





2459-1-003 CIP



Where:

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> = H, CH<sub>3</sub>, X (halogen: F, Cl, Br, I), OH, SH, or NH<sub>3</sub><sup>+</sup>

R<sub>4</sub> = alkyl, aryl

Figure 12